REMARKS

Claims 1-4, 6-8, 10-14, and 16-18 are pending. Applicants have cancelled claims 10 and 11 without prejudice to pursuing this subject matter in one or more continuing applications. Applicants have added new claim 19. Claims 1-4, 6-8, 12-14, 16-18, and 19 will therefore be pending upon entry of the proposed amendments.

Applicants acknowledge that the Examiner has allowed claims 1-4, 6-8, 13, 14, and 16-18.

Applicants have rewritten claim 12 in independent form. As such, claim 12 as presently amended is directed to a method of treating asthma or rhinitis, which includes administering to a patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt as defined in claim 1.

Support for new claim 19, which is directed to a method of producing a CRTh2 receptor inhibitory effect in a patient, can be found throughout the specification, e.g., page 11, lines 8-15 and page 30, line 22 through page 31, line 31.

No new matter is introduced by these amendments.

Rejections under 35 U.S.C. § 112, first paragraph

[I] Claims 10-12 are rejected for allegedly failing to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph.

Applicants respectfully disagree with the grounds for rejection; however, to expedite prosecution of the present application, Applicants have cancelled claims 10 and 11, thus rendering the rejection of these claims moot.

Applicants respectfully request reconsideration and withdrawal of the rejection of claim 12 in view of the aforementioned amendments to claim 12 and the following remarks. Claim 12 as presently amended is directed to a method of treating asthma or rhinitis, which includes administering to a patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt as defined in claim 1.

[1] The Federal Circuit discussed the purpose of the enablement requirement of 35 U.S.C. § 112, ¶1 in *Warner-Lambert Co. v. Teva Pharmaceuticals USA, Inc.* 418 F.3d 1326, 1336-1337 (2005) (underline emphasis added):

> The purpose of this requirement is to ensure that 'the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims.' *Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195-96 (Fed.Cir.1999); see also Donald S. Chisum, 3 Chisum on Patents § 7.01 (2002).

The Federal Circuit in *Warner-Lambert* stressed that the specification must teach one how to make and use the claimed invention without undue experimentation (*Id.* at 1337, emphasis added):

> Accordingly, we have held that the specification must provide sufficient teaching such that one skilled in the art could make and use the full scope of the invention without undue experimentation. *[citations omitted]* 'The key word is 'undue,' not experimentation." *Wands*, 858 F.2d at 737 (citation omitted). **That is, the specification need only teach those aspects of the invention that one skilled in the art could not figure out without undue experimentation**. See, e.g., *Nat'l Recovery Techs.*, 166 F.3d at 1196 ('The scope of enablement ... is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation.'); *Wands*, 858 F.2d at 736-37 ('Enablement is not precluded by the necessity for some experimentation such as routine screening.').

[2] The specification teaches a genus of phenoxyacetic acid compounds that are capable of modulating CRTh2 receptor activity. Such compounds are claimed in claims 1-4, 6-8, 13, 14, and 16-18, which according to the Office Action, are allowed. In addition:

[A] The specification teaches one how to both synthesize and administer the claimed compounds (specification, e.g., at page 5, line 24 through page 11, line 6; page 16, line 12 through page 23, line 28; and the numerous synthesis examples beginning at page 24). The specification also provides an art recognized *in vitro* assay that can be used to evaluate the claimed compounds' ability to inhibit CRTh2 receptor activity. The CRTh2 receptor, ligands for this receptor, as well as the aforementioned inhibitory assay were known in the art as of Applicants' filing date.

[B] The specification teaches that the claimed compounds are capable of inhibiting CRTh2 receptor activity. More specifically, the specification teaches (page 31, lines 30-31):

> Compounds of formula (I) have an IC_{50} value of less than (<) 10μM.
> Specifically, example 2 has a $pIC_{50} = 7.1$ and example 3 has a $pIC_{50} = 6.6$.

The Office has provided no specific evidence that the observed *in vitro* effect fails to show predictability or is not relevant.

[C] The nexus between (1) inhibition of CRTh2 receptor activity and (2) asthma, rhinitis, and the treatment of these two disorders was established (and arguably well established) as of Applicants' filing date. This is discussed in detail in the Background[1] section of the specification (page 1, lines 7-12, emphasis added):

> EPA 1 170 594 discloses methods for the identification of compounds useful for the treatment of disease states mediated by prostaglandin D2, a ligand for orphan receptor CRTH2. GB 1356834 discloses a series of compounds said to possess anti-inflammatory, analgesic and antipyretic activity. It has been found that certain phenoxyacetic acids are active at the CRTH2 receptor, and as a consequence are expected to be potentially useful for the treatment of various respiratory diseases, including **asthma** and COPD.

and in EP 1 170 594 (a copy of which is included in the Information Disclosure Statement filed herewith); see, e.g., the abstract; page 2, lines 47-49; page 4, lines 26-32; and page 5, lines 27-34. Both asthma and rhinitis are specifically mentioned in EP 1 170 594. Since the claimed compounds are capable of inhibiting CRTh2 receptor activity, the skilled artisan at the time of filing would therefore have reasonably predicted that the claimed compounds would have been useful for treating, at the very least, asthma and rhinitis.

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[1] The Federal Circuit in *Callicrate v. Wadsworth Mfg., Inc.* 427 F.3d 1361, 1374 (2005) held that the background section of a patent specification can enable a feature of a claimed invention: "First, a patent specification may sufficiently enable a feature under § 112, ¶ 1, even if only the background section provides the enabling disclosure."

The Federal Circuit in *In re Wright* 27 USPQ2d 1510, 1513 (1993) discussed the requirements for rejecting a claim under the enablement requirement of 35 U.S.C. § 112, first paragraph (emphasis added):

> When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.

Applicants submit that the Office has not met this burden because, at the very least, the Office has not identified any aspect of the claimed methods that a person of ordinary skill in the art "could not figure out without undue experimentation" (*Warner-Lambert Co. v. Teva Pharmaceuticals USA, Inc.* 418 F.3d 1337). The skilled artisan could evaluate the ability of Applicants' novel and nonobvious claimed compounds to treat asthma or rhinitis by synthesizing a candidate compound of the claims and subjecting that compound to an art-recognized assay for treating asthma or rhinitis. Of course, this is **not** to say that the specification does not establish a nexus between the claimed compounds and the treatment of the diseases recited in claim 12 as presently amended. Rather, establishing the nexus apparently sought by the Office falls within the purview of routine screening, which in and of itself does not preclude enablement (*see Wands*, 858 F.2d at 736-37).

Thus, the specification provides sufficient teaching such that a person of ordinary skill in the art could practice the claimed methods without undue experimentation.

In view of the foregoing, Applicants respectfully request that the 35 U.S.C. § 112, ¶1 rejection be withdrawn.

[II] Applicants respectfully request that the rejection not be applied to new claim 19, which is directed to a method of producing a CRTh2 receptor inhibitory effect in a patient, which includes administering to the patient an effective amount of a compound of formula (I) as claimed in claim 1 or a pharmaceutically acceptable salt thereof.

[1] The specification teaches a genus of phenoxyacetic acid compounds that are capable of inhibiting CRTh2 receptor activity. Such compounds are claimed in claims 1-4, 6-8, 13, 14, and 16-18, which according to the Office Action, are allowed.

[2] The biological data for the claimed compounds, as presented in the specification, is reproduced below (page 31, lines 30-31):

> Compounds of formula (I) have an IC_{50} value of less than (<) 10μM.
> Specifically, example 2 has a pIC_{50} = 7.1 and example 3 has a pIC_{50} = 6.6.

As can be seen, the results of the binding assay are presented as **IC_{50} values**, which are **inhibitory** concentrations. Qualitatively, the IC_{50} for a substance (e.g., a drug) is a measure of the substance's effectiveness in inhibiting a particular biological process. Quantitatively, the IC_{50} for a substance is the concentration of the substance needed to inhibit the particular biological process by 50%. In some instances, IC_{50} values are also converted to the pIC_{50} scale (-log IC_{50}), in which higher values indicate exponentially greater potency. Data expressed in this format can be found in the specification at page 31, line 31. Here, the IC_{50} values reported in the specification indicate the concentration (<10μM) of claimed compound at which 50% of the inhibitory effect on the uptake of prostaglandin D2 is achieved. As explained above, each of the pIC_{50} values reported for the claimed compounds is the negative log of the IC_{50} value for that particular compound. Thus, the skilled artisan would understand that the claimed compounds are capable of inhibiting CRTh2 receptor activity and would reasonably expect that the claimed compounds would be capable of producing a CRTh2 receptor inhibitory effect in a patient.

[3] Finally, and as discussed above, the specification teaches one how to both synthesize and administer the claimed compounds.

Accordingly, the skilled artisan would be able to practice the method claimed in claim 19 without undue experimentation.

No fee is believed due. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 06275-472US1 / 101017-1P US.

Respectfully submitted,

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